

### ABSTRACT

The present invention relates to mutant oncolytic vaccinia viruses and their use for selective destruction of cancer cells. The mutant vaccinia viruses of the invention include those having a reduced ability to inhibit the antiviral dsR-NA dependent protein kinase (PKR) and increased sensitivity to interferon. Such mutants include, for example, vaccinia viruses having mutations in the E3L and/or K3L regions. The invention is based on the discovery that vaccinia viruses having mutations in the E3L region are capable of replication in oncogenic cells resulting in cell lysis. The invention further provides methods for treating proliferative disorders, such as neoplasms, in a host comprising administration of mutant vaccinia virus under conditions which result in substantial lysis of the proliferating cancer cells.